Lactose intolerance: nutritional implications

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Summary

Occurrence and metabolism of lactose
Lactose or milk sugar is a disaccharide consisting of the mono sugars galactose and glucose. It occurs only in the milk of mammals. Newborns possess in their intestine an enzyme, called beta-galactosidase or lactase, which can break down lactose into its monosaccharide components galactose and glucose. Subsequently these mono sugars are actively absorbed and transported to the liver via the portal vene. In the liver galactose is converted into glucose. Glucose can easily serve as a fuel for the body cells.

Lactose intolerance
In all mammals and also in about 70% of the world population the lactase activity in the intestine decreases after the weaning period. This decrease is genetically programmed and is not caused by the decrease of lactose intake. Only in people of Caucasian origin (Europeans and their descendents oversea) and in people of some isolated African tribes the lactase activity remains at a relatively high level throughout life. The decrease in lactase activity may result in signs of lactose intolerance upon the ingestion of lactose. These signs include intestinal cramps, bloating, flatulence and sometimes osmotic diarrhea. Lactose intolerance is caused by the fermentation of undigested lactose by the intestinal flora. Fermentation products include lactic acid and volatile fatty acids, (which increase the osmotic value of the intestinal contents) and gasses (mainly carbon dioxyde and hydrogen).

Implications of lactose intolerance
It is nowadays generally accepted that a decrease of the lactase activity after the weaning period should not lead to the conclusion that lactose ingestion be discouraged in those people with low lactase activity. The reason is that moderate amounts of lactose, and especially when distributed over the day across meals, are well tolerated by children and adults who have demonstrated to be lactose intolerant in a typical traditional lactose intolerance test. So under these circumstances amounts of 10-15 g of lactose, corresponding to approx. 250-300 ml of cow's milk can be consumed without any symptoms of lactose intolerance. Even in children recovering from diarrheal diseases, lactose ingestion after oral rehydration therapy needs not to be discouraged.

Special nutritional effects of lactose
Lactose is actually a very special sugar. In human milk it contributes to the development of the so called bifidus flora in the infant. A bifidus flora is an intestinal flora which is dominated by Bifidobacteria. Bifidobacteria increase the colonization resistance in the intestine against pathogenic microorganisms. Lactose also improves the utilization of minerals, especially calcium, magnesium and zinc. It is also less sweet and less cariogenic than several other sugars, including sucrose, glucose and fructose. In addition lactose ingestion results in a lower glycaemic response than for instance sucrose and glucose. Therefore lactose is a suitable sugar in the diabetic diet.

Adverse effects of lactose

Several publications about negative health effects of lactose ingestion have been published the last 10-15 years. These effects include cataract formation and ovarian cancer development. Cataract formation upon lactose ingestion could indeed result from a disturbance in the biochemical conversion of galactose into glucose and consequent accumulation of galactitol in the lens of the eye. However, there is no evidence for a link between lactose ingestion and cataract formation in people with normal liver functions. With respect to a link between lactose consumption and ovarian cancer formation, it has been speculated also that decreased liver conversion of galactose raises the blood galactose level which could cause ovulatory dysfunction and an increased secretion of gonadotrophic hormones leading to a raised ovarian cancer risk. Since, however, there is no evidence that galactose increases ovulatory dysfunction, the relation between lactose and ovarian cancer risk remains speculative.

Contents

1. Introduction

1.1 Lactose and lactose intolerance

Lactose is a disaacharide (4 -β - D - galactosyl - D - glucose) which occurs only in the milk of mammals. The lactose content of human milk is about 7 g per 100 ml and that of cow's milk is about 4.8 g per 100 ml. After ingestion lactose is broken down in the intestine into its monosaccharide components galactose and glucose, mainly by a β-galactosidase which is bound to the mucosal membrane. After splitting, these monsaccharides are actively absorbed and transported to the liver via the portal blood vessel. If lactose is not broken down into galactose and glucose, it escapes digestion in the small intestine and reaches the caecum and colon where it is fermented by the microflora. This fermentation results in the formation of short chain fatty acids, lactic acid and gasses (carbon dioxyde, hydrogen and methane). This raises the osmotic value of the intestinal contents and causes diarrhea. The gass production causes flatulence and bloating. Diarrhea, flatulence, bloating and intestinal cramps are the well-known signs of lactose intolerance. The prevalence of lactose intolerance, particularly in many developing countries, has raised many questions about the suitability of cow's milk or cow's milk powder as food supplements in food aid programmes.

1.2 Aim of the monograph

It is the aim of this monograph to review existing knowledge about lactose intolerance. After a discussion of the digestion of lactose, this monograph deals with the diagnosis, prevalence and causes of lactose intolerance. The nutritional implications of lactose intolerance are discussed. Finally attention is given to the nutritional significance of lactose.

2. Digestion of lactose and lactose malabsorption

2.1 The brush border lactase

At birth mammals possess in their small intestine, particularly in the jejunum, two β-galactosidases (lactases), one extracellular which is bound to the mucosal membrane, and one intracellular in the lysosomes and cytoplasma of the intestinal epithelial cells. The latter enzyme, however, does not play an important role in the break down of lactose. The brush border lactase is present already in the foetus since the second half of pregnancy and reaches its maximum activity very shortly after birth. Normally in mammals, thus also in humans, the activity decreases after the weaning period. Remarkably, only those humans belonging to the Caucasian (West European) race and to some isolated Indian and African tribes (in total approx. 20% of the world population) maintain throughout life a high lactase activity in their intestine. The normal decrease of the lactase activity is genetically programmed and is not caused by stopping the lactose ingestion after the weaning period.

2.2 Hydrolysis of lactose and absorption of glucose and galactose

Lactose exists in two isomeric forms, alpha and beta, differing in configuration of the hydroxy group in position 1 of the glucose moiety (see figure 1)

Lactose (α vorm)
(4-0-β-D-galactosylpyranosyl-α-D-glucopyranoside)

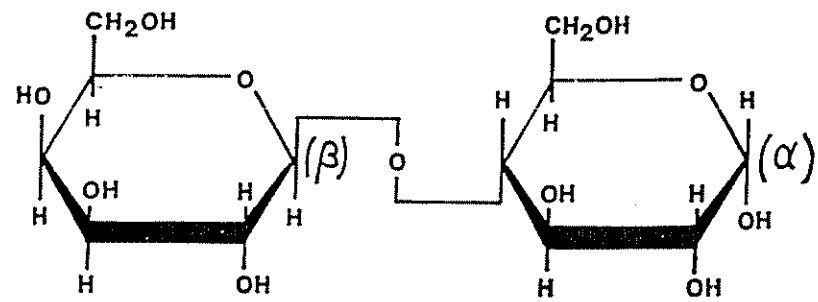

Figure 1.
α-lactose (4-0-β-D-galactosylpyranosyl-α-D-glucose)

In aqueous solution alpha and beta lactose exist in equilibrium with approximately 63% of the lactose in the beta form. After its ingestion lactose is broken down by the brush border lactase into galactose and glucose. Both sugars share a common absorption pathway and they are the only monosaccharides that are actively absorbed. The lactase prefers the β-isomeric form of lactose as substrate and this causes a shift in the equilibrium between α- and β-lactose in favour of the latter (mutarotation).

2.3 Conversion of galactose into glucose

After transport via the portal vessel to the liver, galactose is converted into glucose according to the so called Leloir pathway. This conversion requires three enzymes , e.g. galactokinase (E1), galactose-1-phosphate uridyltransferase (E2) and uridine diphosphogalactose-4-epimerase (E3). The respective reactions are given below.

Gal + ATP	-------E1----------	Gal-1-P + ADP
Gal-1-P + UDPGluc	-------E2----------	UDPGal + Gluc-1-P
UDPGal	-------E3----------	UDPGluc

2.4 Terminology of lactose intolerance disorders

A lot of confusion exist about the terminology which has been used in the literature of lactose intolerance. Therefore a brief summary is given of the different terms that have been used and what these terms mean.

2.4.1 Congenital lactase deficiency

Congenital lactase deficiency is a rare disease (inborn error of metabolism), occurring sometimes in newborn infants. Up to 1983 a total of 30 patients had been described, 16 of these had been found in Finland (Dahlquist, 1984).

2.4.2 Lactase non-persistence

In approximately 90% of the world population the activity of the brush border lactase declines after early childhood to about 5-10% of its pre-weaning level. This decrease is genetically programmed and occurs at different ages in different populations. It is called "lactase non-persistence" (Dahlquist, 1984). Lactase non- persistence fits well in the general pattern of lactase activity decrease, seen in mammals. Other terms for lactase non-persistence are *hypolactasia*, and *primary adult lactase deficiency*. In this latter term the word "deficiency" is actually not correct, since the genetically programmed age-associated decrease of lactase is a dominant phenomenon in mammals and can therefore not be considered as a deficiency. For that reason it is better to use the terms "lactase persistence" and "lactase non persisten-

ce" for (adult) lactase-positive persons and lactase-negative persons respectively. Why the decrease of lactase activity occurs at different ages in different populations is not known. According to Cook (1967) Bantu children have lost almost all of their lactase activity at the age of four years and similar observations have been made for children in Thailand (Keusch et al., 1969) and Jordania (Hijazi et al., 1981), wheras in Finland the decrease has been repoted to occur between ages 10 and 20 (Sahi et al., 1983), and in Israel between ages 6.5 and 8 (Gilat et al., 1974). For North American Indian children lactose malabsorption was assessed at age 5 (Newcomer et al., 1977). Taking into account the existence of two different enzyme systems, it is possible that several genes code for lactase activity. The brush border lactase could disappear first (at about 3 years of age) and the intracellular enzyme later.

2.4.3 Secondary lactase deficiency

The age related decrease of lactase activity should be clearly differentiated from a decrease of the lactase activity which is secondary to gastro-intestinal disease. This is called secondary lactase deficiency and is generally temporary. It may be caused by acute gastro enteritis, Giardiasis, coelic disease, protein intolerance (cow's milk, egg, soy), protein energy malnutrition, inflammatory bowel disease, gastro-intestinal surgery, and antibiotic treatment.

2.4.4 Congenital lactose intolerance

Normally only very small amounts of lactose are absorbed intact and this lactose is excreted into the urine, since it cannot be utilized by the body. In a sporadically occurring congenital disease (inborn error of metabolism), lactose is absorbed intact because of an abnormal permeability of the gastric mucosa. This causes vomiting, failure to thrive, lactosuria, dehydrdation and acidosis early in life after ingestion of lactose. The disease becomes fatal if untreated (Dahlquist, 1984). Up to 1981 fewer than a dozen patients had been described.

2.4.5 Lactose intolerance

Lactose intolerance involves the appearance of clinical symptoms (intestinal cramps, flatulence, nausea, bloating, diarrhea) following the ingestion of a standard dose of lactose in water solution (usually 50 g of lactose in adults or 2 g of lactose per kg body weight in children) in a lactose tolerance test (LTT).

2.4.6 Milk intolerance

Milk intolerance involves the appearance of clinical symptoms of lactose intolerance or of immunlogical (allergic) reactions to cow's milk proteins, following the ingestion of milk. Milk intolerance should be clearly differentiated from lactose intolerance, since (1) nutritionally significant amounts of milk may be tolerated by persons who are considered as lactose intolerant by a standard lactose tolerance test and (2) since milk intolerance may be caused by cow's milk protein allergy.

2.4.7 Lactose-malabsorption

Lactose malabsorption refers to the situation that lactose absortption is disturbed, as a consequence of congenital lactase deficiency, secondary lactase deficiecy or lactase non persistence (hypolactasia). We prefer the term lactose malabsorption over the term lactose intolerance since it appeared that malabsorption at lower intake levels does not cause lactose intolerance symptoms in lactase non-persistent subjects. Or in other words lactose intolerance is a dose dependent phenomenon.

2.5 Summary of lactose intolerance

The different causes of lactose intolerance can be summarized as follows (Dahlquist, 1984):

Congenital forms:	
Congenital lactase deficiency	Rare disease occurring in infants Inborn error of metabolism
Familial lactose intolerance	Abnormal permeability of gastric mucosa to disaccharides Inborn error of metabolism
Acquired forms:	
Adult primary lactase	Non persistency of lactase deficiency after (hypolactasia) childhood. Nor mal situation in more than 75% of world population
Secondary lactase deficiency	Damage to intestinal mucosa as a consequence of disease. Generally temporarily

3. Diagnosis of lactose malabsorption

Lactose malabsorption can be diagnosed by several tests. The most well-known tests are the Lactose Tolerance Test (LTT), the Breath Hydrogen Test (BHT), and the measurement of lactase activity in a brush border sample of the intestine (Luyken and Zaal, 1977; Leegwater-van der Linden, 1985; Dahlquist, 1984).

3.1 The lactose tolerance test

In the LTT gastro-intestinal symptoms of lactose intolerance are recorded and the capillary blood glucose level is measured at various time points following the oral ingestion of 50 g of lactose in a aquous solution (or 2 g of lactose per kg body weight in the case of children) on a empty stomach (see Figure 2).

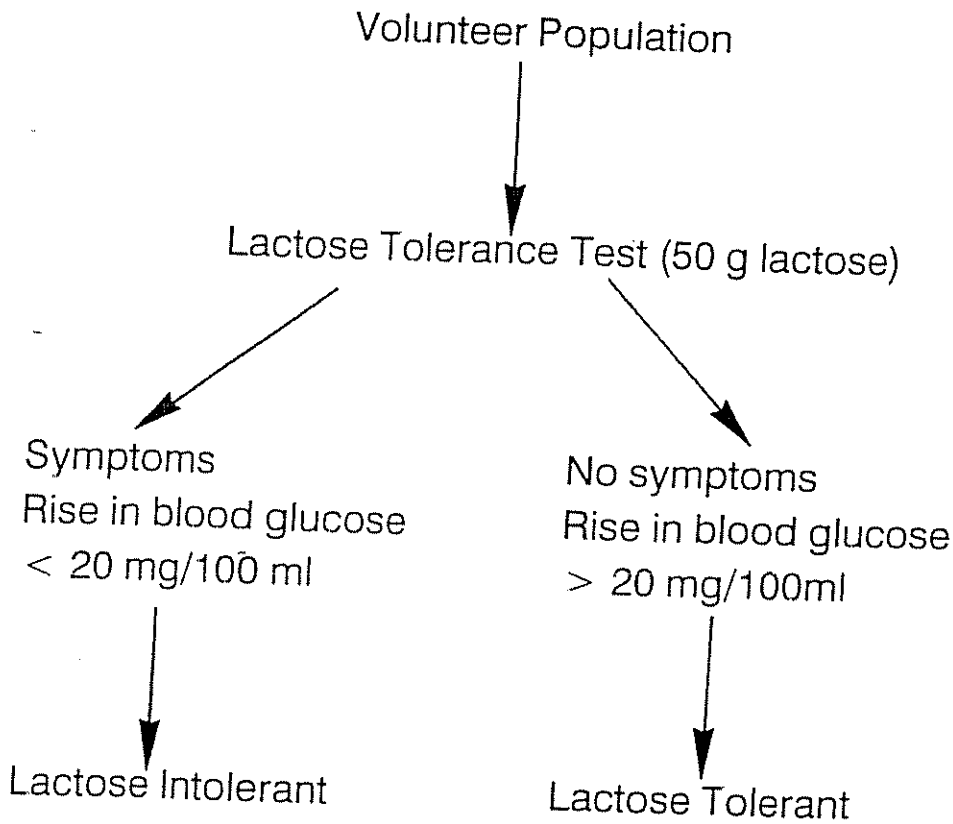

Figure 2
Schematic presentation of the lactose intolerance test.

A flat curve (blood glucose level rises less than 20 mg/100 ml) reflects lactose malabsorption. The test has been used frequently until about 1980 to investigate the geographical distribution of hypolactasia. The physiological significance of the LTT test is very limited, firstly because a 50 g dose of lactose corresponds to the intake of more than 1 liter of milk, a volume which is normally not taken at once and secondly, since tolerance to lactose is much higher when the sugar is taken in combination with a meal (see chapter 5).

3.2 The breath hydrogen test

The principle of the BHT is based on the formation in the terminal intestine of H2 by the intestinal flora from undigested lactose and the excretion of this gas in the breath. After fasting overnight 50 g of lactose is given in a aquous solution. Before - and at various time points after adminstration breath samples are taken and analyzed for H2. An increase in breath H2 of more than 20 ppm indicates lactose malabsorption. This test is very simple. Although it has some drawbacks, it has largely replaced the classical LTT. Again, as for the LTT, the physiological significance of a positive test is limited, e g. a positive test does not mean that lower doses of lactose could not be tolerated without symptoms.

3.3 Measurement of brush border lactase

Measurement of the brush border lactase activity is an invasive test, which requires the obtaining of a mucosal scraping. Generally such a scraping is taken from the jejunum. prefereably 20 cm after the Treitz ligament. Lactase activity in the scraping is performed according to the method by Dahlquist. If the activity is lower than 1-2 Units per g mucosa lactase deficiency is prevalent. The disadvantage of the method is that a mucosal scraping includes only a very small surface area of the small intestine and needs not be representative for the whole surface.

3.4 Other methods

Other methods, used to diagnose lactose malabsorption, are an X-ray investigation - after ingestion of 25 g lactose together with barium sulphate to measure intestinal transit time (shortened in the case of lactose malabsorption), laboratory investigation of urine (presence of lactose) and faeces (decreased pH, increased concentration of lactic- and organic acids, presence of reducing substances), and the measurement of the blood galactose concentration after lactose ingestion combined with alcohol (0.3-0.5 g per kg body weight). The latter method is based on the inhibition of galactose metabolism in the liver by alcohol. It is also possible to perform an absorption test with ^{14}C-labeled lactose.

4. Geographical distribution of lactose intolerance

Adult primary lactase deficiency (or preferably lactase non-persistence) is widely distributed in the world. It is programmed by an autosomal gene with a recessive allele for lactase deficiency and a dominant allele for lactase persistency. Lactose malabsorption does not occur frequently in West Europeans (and their oversea descendents), in North Africa, parts of India and in the Middle East. In other parts of the world its prevalence is estimated between 70 and 100%. It is estimated that about 70% of the world population demonstrates lactase non-persistence (Anonymous, 1985). Asians and negroes demonstrate 100% lactase non- persitence. Since the geographical distribution of lactase persistency parallells the parts of the world where traditionally milk was a part of the diet (since 4000 BC), Simoons (1981) put forward the hypothesis that lactase persistency developed in societies where milk was an essential supplement to the diet. In those societies where milk was fermented (lower lactose content, micobial lactase activity), the lactase persistency did not provide this selective advantage (parts of India, Egypt, Turkey, South of Africa). Table 1 shows a detailed overview of the geograpgical distribution of lactase non persistence.

Table 1. Geographical distribution of lactase non-persistence (adult primary lactase deficiency)

Population	% lactase non-persistence	Population	% lactase non-pesistence
Europe		Asia	
Finns	15	Judes	62-84
Danes	3	Thais	1
Cypriotes	88	Indonesians	91
Britons	6	Chinese	100
Germans	10	Japanese	100
		Koreans	100
Africa		Fillipino's	100
Ugandese		Indies	50
Tutsi	14		
Bantu	85	America	
North Nigerians	20	North America	
South Nigerians	99	Indians	88
Egypts	90	Eskimo's	80
Kenyans	62	Whites	6-7
Arabs	81	Blacks	70-77
Australia		South America	
Papuans	100	Indians	100
Natives	85	Peruans	85
Whites	6		

Taken from De Cuyper (1991)

5. Nutritional factors and lactose malabsorption

As stressed in Chapter 2, lactose intolerance is a dose dependent phenomenon. The wide geographical distrubution of lactase non-persistence should not be explained in the sense that lactose consumption in lactase non-persistent subjects will always lead to signs of lactose intolerance. On the contrary, it is generally accepted that a certain threshold level of lactose is needed to initiate symptoms.
Whether or not symtoms will develop depends on the rate of entry of lactose into the colon, the rate of fermentation and the rate of absorption of fermentation products. Symptoms will devellop when the rate of lactose entry exceeds the rate of fermentation of when the rate of fermentation exceeds the rate of absorption of fermentation products. The threshold level will depend on various factors. These include:

- the remaining mucosal lactase activity,
- the intestinal transit time,
- the distribution of lactose intake over the day,
- the coingestion of a meal,
- lactase activity in food, e.g. yogurt

5.1 Coingestion of a meal

Coingestion of a meal will cause a slow-release effect of lactose into the duodenum and is associated with increased tolerance (Martini and Savaiano, 1988).
These investigators observed in 12 lactose-malabsorbing subjects that ingestion of a standard breakfast (two slices of whole-wheat bread, 32 g peanut butter, 20 g strawberry jelly, 177 ml orange juice and a small banana) together with 20 g lactose in 435 g milk reduced hydrogen excretion several fold as compared to the ingestion of the milk only. Similarly Solomons et al. (1985) (see Figures 3 and 4) demonstrated a net reduction of 47 % in lactose malabsorption when lactose malabsorbers added solid foods to milk. They postulated that a slower rate of colonic lactose fermentation is the basis for reducing gastro-intestinal symptom when solid foods are combined with milk. Another factor which improves tolerance is the microbial lactase activity in some fermented dairy products, including yogurt (Schaafsma, 1993).

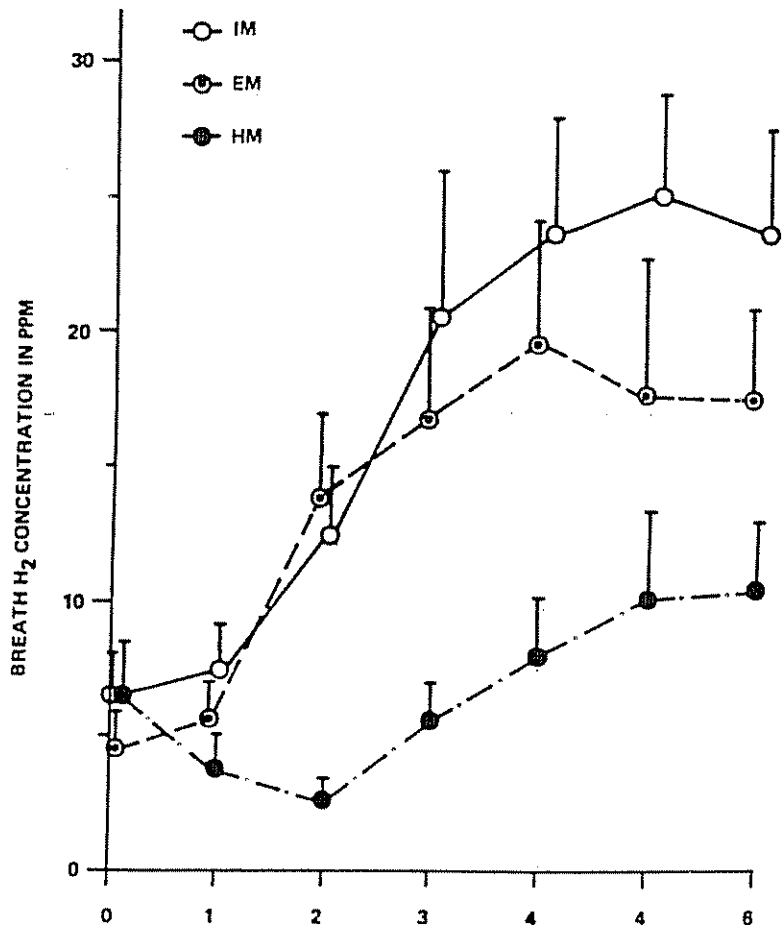

Figure 3.
Mean breath H_2 concentration (± SEM) in ppm at 60-min intervals over 6 hours in 13 lactose-malabsorbers after ingestion of a standard meal with 360 ml milk (-0-), prehydrolyzed milk (-●-), or milk to which 10 drops of a lactase had been added 5 min prior to consumption (-o-). Taken from Solomons et al.(1985)

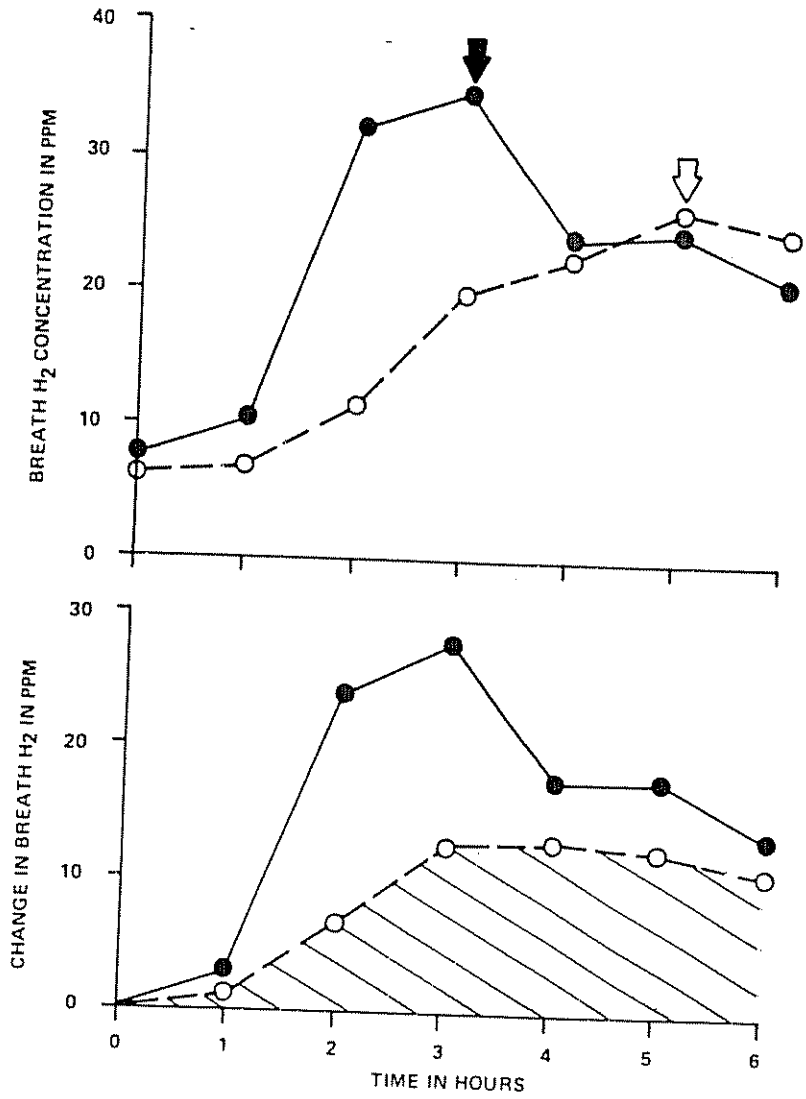

Figure 4.

Upper panel: postprandial breath hydrogen concentration in 13 lactose intolerant subjects after the ingestion of 360 ml milk, containing 18 g lactose (●-●) or this volume of milk combined with a meal (o-o); arrows indicate the shift in time of the peak value, caused by the meal. Lower panel: changes of prost prandial breath hydrogen concentrations of the same experiment, but values are corrected for the effect of the meal as such. Taken from Solomons et al. (1985).

5.2 Effects of lactose dose

In a non-controlled study Bayless et al. (1975) concluded that the majority of people with lactose malabsorption have appreciable symptoms after drinking 240 ml of milk (11 g of lactose), wheras in a a double blind study with adult lactase-deficient subjects 5 g of lactose (in milk or water) was usually tolerated and 10 g gave symptoms (Andersson et al., 1973). Some lactose non-persitent subjects can tolerate higher amounts of lactose, possibly because of adaptation of their intestinal flora (Dahlquist, 1984). In a recent carefully designed blinded cross-over experiment Suarez et al (1995) investigated the appearance of symptoms of lactose intolerance in 21 established adult lactose malabsorbers upon the ingestion of 240 ml of milk combined with breakfast. It was concluded that this volume of milk did not cause to a significant extent signs of lactose intolerance. The 21 lactose - malabsorbing subjects were selected from a group of 30 subjects who had all reported to develop symptoms after the ingestion of less than 240 ml milk. 9 of these 30 subjects appeared to be lactose absorbers in a lactose absorption test. In comparable study Johnson et al. (1993) investigated digestion of lactose and lactose tolerance in 164 African American, aged between 12 to 40 years. All claimed intolerance to a volume of 240 ml or less of milk. In a test with 25 g of lactose in water 50% of the subjects were classified as malabsorbers and lactose intolerant on the basis of hydrogen expiration and development of symptoms, 8 percent were malabsorbers but tolerant, 15% were absorbers but intolerant and 27% were absorbers and tolerant. A further double blind cross-over test on milk intolerance in 45 malabsorbers, who were intolerant to 25 g of lactose, was performed. Subjects were given 315 ml of either lactose containing- or lactose hydrolyzed milk. 67% of the subjects reacted appropriately to presence or absence of lactose in ingested milk, whereas 33% reported symptoms to both the lactose containing and lactose hydrolyzed milk. These results indicate that the cause of milk intolerance in many as one third of African Americans cannot be its lactose content.

5.3 Effects of fermented dairy products

On the basis of many studies reported in the literature, Schaafsma (1993) draw the following conclusions:

1. Symptoms of lactose intolerance and breath hydrogen excretion are substantially reduced after the intake of unheated yogurt as compared to milk.
2. The increased lactose tolerance is associated with an improved lactose digestion.
3. The improved lactose digestion is attributable to the activity in the small intestine of the microbial beta galactosidase from the yogurt culture, to an increased gastro-caecal transit time and to a decreased concentration of lactose in the yogurt.
4. Other strains of lactobacilli than those in the yogurt culture, if possessing beta galactosidase activity, may exert beneficial effects on lactose digestion in

lactase-deficient subjects, but it seems to depend on the survival of the beta galactosidase in the GI tract as well as on the resistance of the enzyme to bile.

5.4 Milk in food aid programs

Before it was realized that lactose intolerance, as assessed by the LTT, should not lead to complete elimination of lactose from the diet, milk in food aid programms for the third world was often discouraged. But in 1972 the Protein Advisory Group of the United Nations stated that milk should not be eliminated from food aid programs for reasons of milk intolerance. The Food and Nutrition Board of the of the USA National Research Council and the American Academy of Pediatrics supported this statement. The validity of the statement was nicely demonstrated by Zaal (1977) in Surinam. He supplemented 6-12 year old Surinam's Bushnegro childeren with 250 ml skimmed milk and compared the effect on the increases of fat-free body mass with that of supplementation with 250 ml lactose-hydrolyzed milk and with that of non-supplementation. The best results were obtained with the lactose containing milk.

5.5 Lactose in the diet of children with diarrhea

The question whether or not lactose can have a place in the diet of infants and young children, recovering from diarrhea has given rise to many clinical investigations. A meta analysis by Brown et al. (1994) of 29 of such (randomized) clinical studies revealed that in the vast majority of children with diarrhea there is no objection against continued feeding of lactose containing non-human milks, especially when oral rehydration provided the basis of therapy.

5.6 Conclusion

It can be concluded on the basis of the studies cited above that lactose malabsorbing subjects can tolerate amounts of lactose without intestinal discomfort up to 11 g, if lactose intake is combined with a meal. It is likely that even higher amounts are tolerated when distributed across meals over the day, or taken with (unpasteurized) yogurt. It can also be concluded that there is no need to remove lactose from milk for infants and children recovering from diarrhea.

6. Nutritional aspects of lactose feeding

A relevant question is: "why is lactose the carbohydrate in the milk of mammals"? From a teleological point of view one might argue that lactose ingestion may be associated with beneficial effects for the consumer that are not exerted by other carbohydrates. Indeed several characteristics of lactose could explain its presence in milk. These are the promotion of development of a so called bifidus flora in breast fed infants and positive effects on the intestinal absorption of minerals. Other positive nutritional charateristics of lactose are related to its low cariogenecity and its lower glycaemic index. There are also speculations about some negative points: lactose ingestion has been noted as a factor in cataract formation and as a risk factor for the development of ovarian cancer. As we will see, the evidence for these negative points is virtually too limited to recommend reduction of lactose intake.

6.1 Bifidogenic factor

In breast fed infants the intestinal flora is dominated by bifidobacteria. These bacteria produce organic acids, e.g. acetic acid, and therefore contribute to colonization resistance against intestinal pathogens. It is believed that the high lactose content of breast milk, together with lysozyme, lactoferrin, immunoglobulins, a low buffering capacity and glucoseamine, contributes to the development of a bifidus flora (Verhoef-Verhage, 1994). A part of the ingested lactose will reach the colon and serve as a substrate for the intestinal flora. Bifidobacteria, like lactobacilli, are able to ferment lactose Schulze and Zunft (1991). Also in later life undigested lactose can serve as a substrate for the intestinal flora. Therefore undigested lactose exerts dietary fiber like effects (Schulze and Zunft (1991), similar to those of other soluble dietary fiber sources, like citrus pectins, inulin and fructo- and galacto-oligosaccharides (Gibsen and Roberfroid, 1995).

6.2 Promotion of mineral absorption

Lengemann et al (1957) were the first who demonstrated (in rats) that lactose promotes intestinal calcium absorption. Calcium absorption occurs via two processes: "active" vitamin D dependent calcium absorption, mainly in the proximal part of the intestine through the mucosal cells, and passive (diffusional) intercellular calcium absorption along the whole small intestine and colon (Anderson, 1991). It is the passive component of the the transport system that is stimulated by lactose. In vitamin D-deficient rats lactose promotes not only calcium absorption but also magnesium and zinc absorption and bone mineralization (Schaafsma et al., 1988); Ziegler and Fomon, 1983; Andrieux and Sacquet, 1983; Gregner et al., 1990). These lactose effects are well-documented in rodents. The significance of lactose in (adult) human diets with respect to mineral utilization remains controversial.

6.3 Low cariogenecity

Of the different dietary sugars, sucrose appears to be the most cariogenic. Glucose and maltose may be marginally less so. According to a UK report on Dietary Sugars and Human Disease (Department of Health, 1989) lactose and galactose are substantially less cariogenic than other sugars. Recently it was stated in a review of recent UK recommendations on Diet and Caries that "as a food constituent, only lactose stands out among the major dietary sugars as being of markedly lower cariogenecity" (Edgar, 1993).

6.4 Moderate glycaemic response

Since galactose and glucose share a common "active" absorption route (and thus show competition for absorption) and since galactose has to be converted in the liver to glucose, lactose has a reletively low glycemic index (maximun rise of blood glucose level after oral intake). The glycaemic index of glucose, lactose, fructose and saccharose was estimated at 131, 69, 35 and 91 (Wolever, 1985). Similarly Bachmann et al. (1977) observed a 40-50% lower maximum blood glucose rise after 50 g of lactose than after 50 g of glucose in normal- and diabetes type II subjects. These results indicate that lactose has a nutritional advantage in the diabetic diet when compared to glucose, starch or saccharose.

6.5 Factor in cataract formation

Children having the hereditary deficiency of galactokinase or galactose-1- phosphate-uridyl-transferase have galactosaemia upon ingestion of lactose or galactose and develop cataract on a lactose or galactose containing diet. The cataract is caused by accumulation of galactitol in the lens of the eye. The galactitol is formed by an aldose reductase and the accumulation exerts an osmotic pressure leading to damage of the lens and cataract. Cataract can be induced in rats on diets containing unphysiological amounts of lactose or galactose (Kinoshita, 1974). Simoons (1982) proposed that high milk consumption in some lactase persistent poulations may contribute to senile cataracts. However Bengtsson et al. (1984) found no correlation with lactose intake in a large number of elderly men, having lactose intakes up to 90 g per day. Italian investigators (Rinaldi et al. 1984) observed a high prevalence of lactose tolerance among adults having senile or presenile cataract as compared to controls. However the number of patients (45) and controls (37) was very low and the controls were patients with gastric or duodenal ulcers, which probably influenced the results of the lactose tolerance test. Couet and Debry (1991) reviewed the subject and concluded that if exceptional cases of homozygous enzyme deficiency were excluded, fragmentary data give reason to believe that a risk of cataract, secodary to lactose and galactose ingestion, is present in certain subpopulations. In these population groups, the size of which is unknown, the lens could be exposed to intermittent episodes of hypergalactosemia due to partial

enzyme deficiency in the galactose metabolic pathway, and/or the persistence of a high adult jejunal lactase activity, and/or large and repeated consumption of either whole lactose or easily absorbed lactose (hydrolyzed forms and non-heated yogurt). However, in a French case-control study (Birlouez-Aragan et al., 1993), yogurt was not cataractogenic, whereas, paradoxically, milk ingestion was dose-related with catarct risk in lactose digesters (particularly diabetics), but not in lactose maldigesters. The author thinks that the evidence for a causal relationship between lactose and cataract is not inconsitent, as far as it concerns people with normal capabilities to convert galactose into glucose. The limited evidence originates from case-controll studies. The results of this type of studies have a high risk to be confounded by uncontrolled variables. One major confouder, for instance, may be alcohol intake. Chronic alcohol abuse could easily interfere with galactose metabolism, since alcohol effectively inhibits uridine-diphosphogalactose-4-epimerase (Kern and Heller, 1968). Alcohol will therefore raise the blood galactose levels when combined with lactose consumption

6.6 Factor in ovarian cancer development

Since 1989 several publications addressed the possibility that lactose increases ovarian cancer risk (Cramer et al., 1989; Reichlin, 1989; Harlow, 1991 and Cramer, 1991), merely on the basis of an ecological and a case control study. Like case control studies, ecological studies cannot provide concluding evidence, because of the high probability of confounding of results by uncontrolled variables. Galactose consumption would increase ovarian cancer risk, particularly in women with low levels of blood cell galactose-1-phosphate-uridyl-transferase. It was reported also that the protective effet of oral contraceptive use on ovarian cancer risk was particularly confined to those women who consumed more than 11 g of lactose per day (Harlow et al., 1991). The authors speculated that galactose could cause ovulatory dysfunction and hypergonadotrophic hypogonadism, leading to increased risk of ovarian cancer. The hypergonadotrophic effect of galactose would be reduced by oral contraceptives which are known to lower gonadotrophins. The authors, however, admit that there is no evidence in man that galactose causes ovulatory dysfunction.

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8. Signatures

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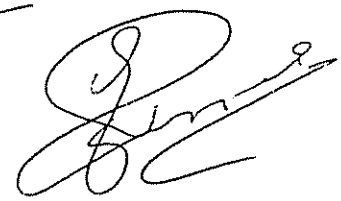

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